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## REMARKS

After entry of this amendment, Claims 1-2 and 4-9 are pending. Claims 10 and 11 have been cancelled in order to further prosecution in view of the finding of the Examiner that the claims are drawn to a nonelected invention. The claims have been amended to more clearly define the invention, and not for patentability reasons. No new matter has been added.

Based on the following remarks, Applicant respectfully requests reconsideration and allowance of the pending claims.

### Rejection of Claims 1,2 and 4-9 under 35 U.S.C. §103(a)

The Examiner rejected Claims 1, 2 and 4-9 under 35 U.S.C. § 103(a) as being unpatentable over Watkins, Jr. *et al.* (*Int. J. Cancer*: 14, 79-807 (1974)) taken with U.S. Patent No. 3,792, 159 to Green *et al.* Applicant respectfully traverses this rejection and requests withdrawal thereof.

The Examiner stated that "Applicant has claimed a method for treating a human with a neoplasm, comprising administering to the human with the neoplasm an effective amount of neuraminidase. Watkins clearly teaches that neuraminidase is administered to humans with a neoplasm. This is all the claim requires. Thus, the claimed invention is obvious over the cited references."

Applicant respectfully submits that there is no teaching in Watkins of administering a composition comprising neuraminidase to humans, with or without a neoplasm. Watkins teaches *in vitro treatment* of tumor cells with neuraminidase and measuring the *in vitro* response of lymphoblasts to such treated cells. See Watkins, Abstract, "Host blood lymphocytes undergo accentuated blastic transformation when cultured with tumor cells pretreated with neuraminidase." See Watkins, p. 800, 3<sup>rd</sup> paragraph, "enzymatic treatment of tumor cells with neuraminidase in acetate-buffered saline, pH 6.5 containing calcium, and measurement of lymphoblastic transformation by pulse tagging with tritiated thymidine. See Watkins, p. 800, 4<sup>th</sup> paragraph, "Test cultures containing host lymphocytes and neuraminidase-treated tumor cells were compared to control cultures containing host lymphocytes and intact sham-treated tumor cells..."

Watkins teaches that patients who were undergoing surgery of large solid tumors or benign tumors were the donors of tumor cells. (See Watkins, p. 800, 1st paragraph). These tumor cells were treated with the enzyme, neuraminidase, to remove sialic acid residues from the surface of the tumor cells. See Watkins, p. 800, 5<sup>th</sup> paragraph, "These findings... indicate that the observed phenomena are the result of cleavage of terminal sialic acid glycoside bonds at the chemically active tumor-cell surface." When these enzyme-treated tumor cells are added to a lymphocyte culture *in vitro*, the lymphocytes undergo a blastic response, as measured by incorporation of radioactive thymidine, presumably into newly synthesized nucleic acids in newly formed cells. This lymphocyte response is shown in Figure 1, p. 802, and is described on page 801, under Results, Lymphoblastic transformation in tumor-cell cultures, "Lymphocyte response as indicated by blastosis index under varying culture conditions is shown in Figure 1 for the group of 38 responding patients." There is absolutely no teaching or suggestion of implanting anything into any of the tumor cell donors.

In the background discussion of Watkins, found on page 799, Watkins cites various articles that show that tumor cells are more immunogenic after treatment with neuraminidase. The only hint of injection into animals is the statement in Watkins that "Animals injected with neuraminidase-treated cells [emphasis added] subsequently show specific resistance to challenge doses of unaltered cells that would have been lethal if injected into untreated animals." Again, there is no teaching or suggestion of administration of a composition comprising neuraminidase to tumor-bearing animals, there is only injection of cells that were pretreated with an enzyme, neuraminidase. ✓

Applicant respectfully submits that a teaching of pretreating tumor cells with an enzyme that remove sugar residues, thus changing the cells so that immune cells respond differently to the treated cells, is in no way a teaching or suggestion of a method of treating neoplasms in humans by administering a composition comprising neuraminidase. There is no teaching or suggestion in Watkins of treating humans with neoplasms, only a teaching of treating neoplastic cells in order to render them more likely to trigger an immune response. ⊗

As-stated by the Examiner, Green "was cited as a general teaching to show the wide use of phenol saline as a solution for injection of biological materials into the

body”, and as such, does not, in combination with Watkins, result in a teaching that renders the currently pending claims obvious. Applicant respectfully requests the Examiner to withdraw the rejection.

Request for Interview

Applicant respectfully requests a personal interview with the Examiner to discuss the currently claimed invention and asks that the Examiner contact Mary Anthony Merchant, Ph.D., attorney of record, at 404-745-2426 to schedule a convenient date and time.

## MARKED COPY OF AMENDMENTS

### Amendments in the Claims

In accordance with 37 C.F.R. § 1.121(c), the following version of the claims as rewritten by the foregoing amendment shows all the changes made relative to the previous version of the claim.

1. (Amended) A method for treating a human with a neoplasm, comprising administering to the human with the neoplasm a composition comprising an effective amount of neuraminidase.

2. (Twice Amended) The method of Claim 1, wherein the composition comprises neuraminidase [is] dissolved in a phenol-saline solution.

4. (Amended) The method of Claim 1, wherein the neuraminidase composition is administered systemically.

5. (Amended) The method of Claim 1, wherein the neuraminidase composition is administered by subcutaneous injection, intramuscular injection, intravenous injection, nasal administration, sublingual administration or transdermal administration.

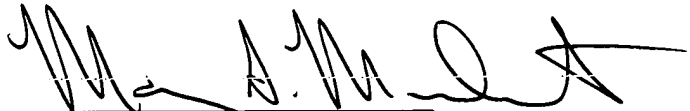
6. (Amended) The method of Claim 5, wherein the neuraminidase composition is administered sublingually.

7. (Amended) The method of Claim 5, wherein the neuraminidase composition is administered nasally.

## CONCLUSION

The foregoing is submitted as a full and complete response to the Office Action mailed June 20, 2002. Applicant respectfully submits that the present application is in condition for immediate allowance. An early notification is earnestly solicited. If the Examiner has any questions, or further issues remain to be resolved, the Examiner is requested to contact the undersigned at 404.745.2426.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Mary A. Merchant', with a stylized flourish at the end.

Mary Anthony Merchant, Ph.D.  
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